REMARKS AND AMENDMENTS

I. THE AMENDMENTS

Applicants have herein amended the specification to comply with the examiner's request to remove embedded hyperlinks (MPEP 608.01). In the claims, please cancel Claim 21 without prejudice or disclaimer. Applicants have amended Claims 15, 16, 17,19, 27 and 29-31 to better point out and describe the invention. Support for the amended claims can be found in the specification at least as follows:

Claim 15- Support for Claim 15 can be found at least in Example 1, "Isolation of cDNA Clones Encoding Human Bolekine" beginning on page 65 of the specification.

Claim 16-Support for Claim 16 can be found at least in Claim 16, and under "Deposit of Material" beginning on page 77, line 19 of the specification.

Claim 17-Support for Claim 17 can be found at least in Example 10, "Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay" beginning at page 73, line 19 to page 74, line 14.

Claim 18- Support for Claim 18 can be found at least in Example 2 "Use of Bolekine-encoding DNA as a hybridization probe" beginning on page 66, line 35 to page 67, line 9.

Claim 19-Support for Claim 19 can be found at least beginning on page 41, line 16 to page 42, line 2.

Claim 27- Support for Claim 27 can be found at least beginning on page 52, line 6 to page 53, line 18.

Claim 29- Support for Claim 29 can be found at least in Example 10, "Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay" beginning at page 73, line 19 to page 74, line 14.

Claim 30-Support for Claim 30 can be found at least beginning on page 52, line 6 to page 53, line 18.

Claim 31- Support for Claim 31 can be found at least beginning on page 52, line 6 to page 53, line 18.

Claim 47-Support for Claim 47 can be found at least beginning in Example 1, "Isolation of cDNA clones encoding human Bolekine", page 65, line 14 to page 66, line 33.

II. THE OBJECTIONS

The Examiner has objected to Claims 27, 29, 30 and 31 as allegedly encompassing non-elected inventions, and require amendment to limit to the elected invention. Applicant has amended the dependance of Claim 27, 29, 30 and 31, to further define the claimed invention.

III. THE REJECTIONS

A. The Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected Claims 15, 17, 19, 20, and 27-31 under 35 U.S.C. § 102(e) as allegedly being anticipated by Ni et al., U.S. Patent No: 5,910,431. Applicants respectfully traverse the rejection. The Bolekine polypeptide as claimed in Claim 15 is novel and unique, as shown in Exhibit B and in the sequence alignment provided by the PTO. Ni et al., teaches on page 25 lines 44-47;

> "Ckα-2 may also be employed to *inhibit* T cell proliferation by the inhibition of IL-2 biosynthesis for the treatment of T-cell mediated auto-immune diseases and lymphocytic leukemias." (Emphasis added).

The Applicants have submitted data in the specification (Example 10, beginning on page 73) that demonstrate that Bolekine has the opposite effect as taught by Ni et al. In T cell assays, the Bolekine polypeptide demonstrated a potent T-cell proliferative effect, and this unexpected result has been incorporated into the claims.

Ni et al., teaches away from using the Bolekine polypeptide to stimulate T cells. Hence, the skilled practitioner would have been led by Ni et al., to believe that one should not use the Bolekine polypeptide to stimulate T cell proliferation, as it would be inhibitory. Where there is a specific statement in the reference, and the reference appears to teach away from the function claimed, there is not the requisite motivation to attempt experimentation of the specific function claimed. Such a teaching-away disclosure provides evidence of non-obviousness. See *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 296 (Fed. Cir. 1985). In light of this asserted novel effect, and the amendments made to the claims, Applicants respectfully request withdrawal of the rejection.

B. The Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected Claim 21 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ni et al., in view of Boyle (USPN 5,843,678). Without agreeing with assertion made by the Examiner, Applicants have cancelled Claim 21 without prejudice or disclaimer, thus obviating the rejection.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

In light of the above amendments and remarks, Applicants believe that this application is now in condition for immediate allowance and respectfully request that this case pass to issue.

The examiner is invited to contact the undersigned at (650) 225-3733 if any issues may be resolved in that manner.

Respectfully submitted,
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PATENT TRADEMARK OFFICE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:
Please replace the paragraph beginning at page 10, line 28 with the following rewritten paragraph:

--Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be [downloaded from http://www.ncbi.nlm.nih.gov or otherwise] obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.--

Please replace the paragraph beginning at page 65, line 15 with the following rewritten paragraph:

--Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be [downloaded from http://www.ncbi.nlm.nih.gov or otherwise] obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.--

Please replace the paragraph beginning at page 65, line 15 with the following rewritten paragraph:

--The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ^{TM}, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation

of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington [; http://bozeman.mbt.washington.edu/phrap.docs/phrap.html]).--

***In the claims*:**

15. (Twice amended) [The] An isolated Bolekine polypeptide comprising amino acid residues 1[or about 34] to [about] 111 of Figure 2 (SEQ ID NO:2).

16. (Amended) [The] An isolated Bolekine polypeptide which is encoded by the cDNA insert of the vector deposited with the ATCC on October 31, 1997 as ATCC Deposit No. 209424 (DNA39523-1192).

17.(Amended) An isolated Bolekine polypeptide comprising the sequence of amino acids from 1[or about 34] to [about] 111 of Figure 2 (SEQ ID NO:2), or a fragment thereof, [sufficient to provide a binding site for an anti-Bolekine antibody] wherein said fragment is capable of enhancing the proliferation of T lymphocytes in a mammal.

19. (Amended) A chimeric molecule comprising [a] the Bolekine polypeptide as in Claim 17, fused to a heterologous amino acid sequence.

27. (Amended) A composition of matter comprising [(a) a] the Bolekine polypeptide as in Claim 17, [(b)an agonist to a Bolekine polypeptide, (c) an antagonist to a Bolekine polypeptide, or (d) an anti-Bolekine antibody,] in admixture with a pharmaceutically acceptable carrier.

29. (Amended) The composition of matter of Claim 27, [(a), (b), (c), or (d)] wherein the Bolekine polypeptide is capable of (i) enhancing the proliferation of T-lymphocytes in a mammal, or (ii) increasing infiltration of inflammatory cells into a tissue of a mammal.

30 (Amended) The composition of matter of Claim 27 comprising a therapeutically effective amount of [(a), (b), (c) or (d)] the Bolekine polypeptide.

31 (Amended) An article of manufacture, comprising:

a container;

a label on said container; and

a composition of matter comprising [(a)] a Bolekine polypeptide of Claim 17, [(b) an agonist of said polypeptide, (c) an antagonist of said polypeptide, or (d) an antibody that binds to said polypeptide,] contained within said container, wherein label on said container indicates that said composition of matter can be used for treating an immune related disease.

--47 (new) An isolated Bolekine polypeptide comprising amino acid residues 34 to 111 of Figure 2 (SEQ ID NO:2).--

APPENDIX A

15. (Twice amended) An isolated Bolekine polypeptide comprising amino acid residues 1 to 111 of Figure 2 (SEQ ID NO:2).

16. (Amended) An isolated Bolekine polypeptide which is encoded by the cDNA insert of the vector deposited with the ATCC on October 31, 1997 as ATCC Deposit No. 209424 (DNA39523-1192).

17. (Amended) An isolated Bolekine polypeptide comprising the sequence of amino acids from 1 to 111 of Figure 2 (SEQ ID NO:2), or a fragment thereof, wherein said fragment is capable of enhancing the proliferation of T lymphocytes in a mammal.

19. (Amended) A chimeric molecule comprising the Bolekine polypeptide as in Claim 17, fused to a heterologous amino acid sequence.

20. The chimeric molecule of Claim 19, wherein said heterologous amino acid sequence is an epitope tag sequence.

27. (Amended) A composition of matter comprising the Bolekine polypeptide as in Claim 17, in admixture with a pharmaceutically acceptable carrier.

28. The composition of matter of Claim 27, which is useful for the treatment of an immune related disease in a mammal.

29. (Amended) The composition of matter of Claim 27, wherein the Bolekine polypeptide is capable of (i) enhancing the proliferation of T-lymphocytes in a mammal, or (ii) increasing infiltration of inflammatory cells into a tissue of a mammal.

30 (Amended) The composition of matter of Claim 27 comprising a therapeutically effective amount of the Bolekine polypeptide.

31 (Amended) An article of manufacture, comprising:

a container;

a label on said container; and

a composition of matter comprising a Bolekine polypeptide of Claim 17, contained within said container, wherein label on said container indicates that said composition of matter can be used for treating an immune related disease.

47 (new) An isolated Bolekine polypeptide comprising amino acid residues 34 to 111 of Figure 2 (SEQ ID NO:2).

APPENDIX B

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p1.bolekine (bolekine),length = 111
p1.Ni (Ni), length = 111


                    10         20         30         40         50
bolekine    MSLLPRRAPPVSMRLLAAALLLLLLALYTARVDGSKCKCSRKGPKIRYSD
            **************************************************
Ni          MSLLPRRAPPVSMRLLAAALLLLLLALYTARVDGSKCKCSRKGPKIRYSD
                    10         20         30         40         50

                    60         70         80         90        100
bolekine    VKKLEMKPKYPHCEEKMVIITTKSVSRYRGQEHCLHPKLQSTKRFIKWYN
            **************************************************
Ni          VKKLEMKPKYPHCEEKMVIITTKSVSRYRGQEHCLHPKLQSTKRFIKWYN
                    60         70         80         90        100

                   110
bolekine    AWNEKRRVYEE
            ******* ***
Ni          AWNEKRRFYEE
                   110
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